## REMARKS

Applicant respectfully requests entry of the remarks submitted herein.

I. The Rejections of the Claims under 35 U.S.C. § 103(a)

The Examiner rejected claims 21-27, 30-32, 34-36, 38-40, 42, 43, 45-54, 57-59, 61-63, 65-67 and 69-71 under 35 U.S.C. § 103(a), alleging that those claims are unpatentable over Deggerdal *et al.* (WO 96/18731; hereinafter Deggerdal) in view of Nargessi (U.S. Patent No. 6,855,499; hereinafter Nargessi). The Examiner also rejected claims 41 and 68 under 35 U.S.C. § 103(a), alleging that those claims are unpatentable over Deggerdal in view of Nargessi and Calbiochem 2000-2001 reagent catalog (hereinafter Calbiochem) and rejected claims 28-29 and 55-56, alleging that those claims are unpatentable over Deggerdal in view of Nargessi and Heath *et al.* (WO 99/39009; hereinafter Heath).

The Examiner also rejected claims 21-26, 30-32, 34-36, 38-40, 42, 43, 45-53, 57-59, 61-63, 65-67 and 69-71 under 35 U.S.C. § 103(a), alleging that those claims are unpatentable over Deggerdal in view of Lader (U.S. Patent No. 6,204,375; hereinafter Lader). The Examiner also rejected claims 41 and 68 under 35 U.S.C. § 103(a), alleging that those claims are unpatentable over Deggerdal in view of Lader and Calbiochem and rejected claims 27-29 and 54-56, alleging that those claims are unpatentable over Deggerdal in view of Lader and Heath.

All of these rejections are respectfully traversed.

The Supreme Court has set out the analysis for patentability under 35 USC 103(a): the scope and content of the cited documents are to be determined; differences between the cited documents and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. (*see, e.g., Graham v. John Deere Co.*, 383 U.S. 1 (1966) and *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007)) Further, the cited documents must be considered in their entirety, and it is not permissible to pick and choose from any one document only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such document fairly suggests to one of ordinary skill in the art. (*see, e.g., Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443, 230 U.S.P.Q. 416 (Fed. Cir. 1986) and *In re Wesslau*, 353 F.2d 238, U.S.P.Q. 391 (C.C.P.A. 1965)) Applicant

submits that the level of ordinary skill in the pertinent art is high. The scope and content of the cited documents and the differences between the cited documents and the claims at issue are discussed hereinbelow, as are the reasons the claims are not obvious in view of the cited documents.

Independent claim 21 recites a method for purifying RNA from biological material comprising RNA, comprising the steps of: (a) mixing said biological material with an RNA Lysing Solution buffered at a pH of greater than about 7, said RNA Lysing Solution comprising an amphiphillic reagent, and an RNA complexing salt, wherein the RNA-complexing salt is an alkali-metal salt present at a concentration greater than about 4 M, wherein said RNA Lysing Solution is free of a strong chaotropic substance; (b) lysing said biological material with said RNA Lysing Solution to form a lysate comprising nucleic acids comprising RNA and non-nucleic acid biological matter; (c) contacting said lysate to an immobilized non-silica solid support, wherein said nucleic acids comprising RNA in said lysate preferentially bind to said solid support; (d) washing said solid support with an RNA wash solution to remove non-nucleic acid biological matter; and (e) preferentially eluting the bound RNA from said solid support with an RNA elution solution to obtain the RNA. Claims 22-32, 34-36, 38-43 and 46-48 depend directly or indirectly from claim 21.

Independent claim 45 recites a method for purifying RNA from biological material, comprising the steps of: (a) contacting a biological material containing RNA with a solid support pre-treated with an RNA Lysing Solution buffered at a pH of greater than about 7, wherein the RNA Lysing Solution is bound to the solid support, said RNA Lysing Solution comprising an amphiphillic reagent and an RNA-complexing salt, wherein the RNA-complexing salt is an alkali-metal salt present at a concentration greater than about 4 M, wherein said RNA Lysing Solution is free of a strong chaotropic substance; (b) contacting said biological material to said solid support in order to release nucleic acids comprising RNA and non-nucleic acid biological matter causing nucleic acids comprising RNA to preferentially bind to said solid support; (c) washing said solid support with an RNA wash solution to remove biological materials other than bound nucleic acids comprising RNA; and (d) preferentially eluting the bound RNA from said solid support with an RNA elution solution to obtain the RNA. Claims 49-59, 61-63 and 65-71 depend directly or indirectly from claim 45.

A. Deggerdal in view of Nargessi

The Examiner rejected claims 21-27, 30-32, 34-36, 38-40, 42, 43, 45-54, 57-59, 61-63, 65-67 and 69-71 under 35 U.S.C. § 103(a), alleging that those claims are unpatentable over Deggerdal in view of Nargessi.

The Examiner states that Deggerdal does not disclose a method in which lithium chloride is included in the lysis solution at a concentration of 4-10 M or a method using cellulose as the solid support (*see* page 5 of the Office Action). As the Examiner states at page 4 of the Office Action, Deggardal does provide solutions in which lithium chloride is present at 0.5 M. Thus, Deggardal discloses a much lower concentration of lithium chloride (0.5 M) than the concentration of salt recited in the pending claims (*i.e.*, greater than about 4 M). Further, Deggerdal goes so far as to state that "a salt may be included to enhance nucleic acid capture, although this is not necessary" (page 8, underline added). In contrast, the presently claimed methods recite the use of an RNA-complexing salt, which is an alkali-metal salt, at a concentration greater than 4 M, which is 8-fold greater than the optional salt concentration described by Deggerdal.

Nargessi relates to methods to bind nucleic acids to magnetizable cellulose (*see* claim 1). Nargessi teaches that in the presence of certain chemicals and salts, formulated as a binding buffer, magnetizable cellulose can adsorb nucleic acids (*see* column 1, lines 46-52). Nargessi states at column 4, lines 9-25 that preferably the salt is NaCl and that salt concentrations in the binding and wash buffers will depend on the salt being used and milieu from which the nucleic acids are to be isolated and purified. Nargessi continues that most preferably, the salt concentration of the binding buffer is about 1.25 M. In the Examples, Nargessi utilizes lysis buffers that do not include LiCl and do include 6 M guanidine-HCl (*see* Examples 3, 5-9, 12, 13, and 16).

Applicant respectfully submits that neither Deggerdal nor Nargessi, either alone or in combination, teaches or suggests a method as claimed that involves the inclusion of an RNA-complexing salt that is an alkali-metal salt present at a concentration greater than about 4 M in the lysing solution. For example, the presently claimed methods recite the use of an RNA-complexing salt, which is an alkali-metal salt, at a concentration greater than 4 M, which is 8-fold greater than the optional salt concentration described by Deggerdal. The lysis solutions of

Nargessi do not involve the use of an RNA-complexing salt, which is an alkali-metal salt, at a concentration greater than 4 M. Further, Nargessi relates to methods and compositions for isolating nucleic acids that involve the use of guanidine-HCl in the lysing solution. In contrast, the claims of the present invention recite that the RNA Lysing Solution is free of a strong chaotropic substance. Thus, Applicant respectfully submits that Nargessi teaches away from excluding strong chaotropic agents from the lysing solution. Accordingly, the claims are not obvious in view of the cited documents, and Applicant respectfully requests withdraw of this rejection of the claims under 35 U.S.C. § 103.

B. Deggerdal in view of Nargessi and Calbiochem

The Examiner rejected claims 41 and 68 under 35 U.S.C. § 103(a), alleging that those claims are unpatentable over Deggerdal in view of Nargessi and Calbiochem. As explained hereinabove, the claims are not obvious in view of either Deggerdal or Nargessi, and the deficiencies of Deggerdal and Nargessi are not remedied by Calbiochem. Accordingly, the claims are not obvious in view of the cited documents, and Applicant respectfully requests withdraw of this rejection of the claims under 35 U.S.C. § 103.

C. Deggerdal in view of Nargessi and Heath

The Examiner rejected claims 28-29 and 55-56, alleging that those claims are unpatentable over Deggerdal in view of Nargessi and Heath. As explained hereinabove, the claims are not obvious in view of either Deggerdal or Nargessi, and the deficiencies of Deggerdal and Nargessi are not remedied by Heath. Accordingly, the claims are not obvious in view of the cited documents, and Applicant respectfully requests withdraw of this rejection of the claims under 35 U.S.C. § 103.

D. Deggerdal in view of Lader

The Examiner rejected claims 21-26, 30-32, 34-36, 38-40, 42, 43, 45-53, 57-59, 61-63, 65-67 and 69-71 under 35 U.S.C. § 103(a), alleging that those claims are unpatentable over Deggerdal in view of Lader.

Deggerdal is described hereinabove.

Lader relates to methods of preserving RNA in intact cells using a preservation media (*see* claim 1). At column 3, lines 47-56, Lader states that the RNA preservation medium can include a salt, and in preferred commercial embodiments, the salt is ammonium sulfate. Lader

states in Example 4 (column 20) that guanidinium isothiocyanate (GITC) is a powerful chaotropic agent used either alone or in conjunction with other reagents in virtually all RNA isolation protocols. Lader uses GITC in Examples in which RNA is isolated (*see, e.g.*, Examples 8 and 21).

Applicant respectfully submits that neither Deggerdal nor Lader, either alone or in combination, teaches or suggests a method as claimed that involves the inclusion of an RNA-complexing salt that is an alkali-metal salt present at a concentration greater than about 4 M in the lysing solution. Even if, for the sake of argument Lader mentions the use of salts, those salts are used in a preservation medium for preserving RNA in intact cells. For example, the presently claimed methods recite the use of an RNA-complexing salt, which is an alkali-metal salt, at a concentration greater than 4 M, which is 8-fold greater than the optional salt concentration described by Deggerdal. Further, Lader relates to methods and compositions for isolating nucleic acids that involve the use of guanidine (*see, e.g.*, Examples 8 and 21). In contrast, the claims of the present invention recite that the RNA Lysing Solution is free of a strong chaotropic substance. Thus, Applicant respectfully submits that Lader teaches away from excluding strong chaotropic agents from the lysing solution. Accordingly, the claims are not obvious in view of the cited documents, and Applicant respectfully requests withdraw of this rejection of the claims under 35 U.S.C. § 103.

E. Deggerdal in view of Lader and Calbiochem

The Examiner rejected claims 41 and 68 under 35 U.S.C. § 103(a), alleging that those claims are unpatentable over Deggerdal in view of Lader and Calbiochem. As explained hereinabove, the claims are not obvious in view of either Deggerdal or Lader and the deficiencies of Deggerdal and Lader are not remedied by Calbiochem. Accordingly, the claims are not obvious in view of the cited documents, and Applicant respectfully requests withdraw of this rejection of the claims under 35 U.S.C. § 103.

F. Deggerdal in view of Lader and Heath

The Examiner rejected claims 27-29 and 54-56, alleging that those claims are unpatentable over Deggerdal in view of Lader and Heath. As explained hereinabove, the claims are not obvious in view of either Deggerdal or Lader and the deficiencies of Deggerdal and Lader are not remedied by Heath. Accordingly, the claims are not obvious in view of the cited

documents, and Applicant respectfully requests withdraw of this rejection of the claims under 35 U.S.C. § 103.

II. The Obviousness-Type Double Patenting Rejection of the Claims

The Examiner provisionally rejected claims 21-32, 34-36, 38-43, 45-59, 61-63, and 65-71 on the ground of nonstatutory obviousness-type double patenting, alleging that those claims are unpatentable over claims 1-85 of U.S. Application Serial No. 11/589,364. As this is a provisional obviousness-type double patenting rejection, Applicant will consider filing a terminal disclaimer should claims of the present application be found otherwise allowable.

## CONCLUSION

The Examiner is invited to contact Applicant's Representative at the below-listed telephone number if there are any questions regarding this Response or if prosecution of this application may be assisted thereby. If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 50-3503. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extension fees to Deposit Account 50-3503.

Respectfully submitted,
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